of our donors at collection sites. More different to gauge, of course, are the self-deferral donors due to this policy. However, we can accurately state the large impact on our RBC supply if a new guideline would restrict the importation of Euroblood. Also, any travel ban that extends to Continental Europe will further erode our donor base of frequent international business travelers.

Euroblood was established some 30 years ago to deal with chronic shortages of blood that were particularly common in large urban areas such as New York City. Currently blood centers in three countries participate, Germany, Switzerland and Holland. The Euroblood centers are FDA approved collection facilities for NYBC. They collect under NYBC's FDA license, use approved SOPs and are routinely inspected by FDA staff. Thus, a unit of blood coming from these Euroblood centers fulfills the exact same criteria as a unit of blood collected locally. Euroblood in the past has provided as much as a third of our area's RBC needs.

With changes in demand for fractionated plasma and internal restructuring of blood programs, the availability of European red cells has declined over the past three years, dropping by about a third to its current level. We have compensated for this loss by increasing our collection rate over 20 percent during this period. Attempts to replace Euroblood with imports from U.S. centers have been'largely

ineffective. Nationwide slow growth in collections and accelerating transfusion demand have created a chronically deficient red cell supply, most seriously, of course, in the now longer and more severe seasonal shortage periods. These shortages are leading to unsettling medical practices in our hospitals. These include delay of 'urgent or elective surgery, postponement or reductions of transfusions for cancer patients, and transfusion of Rh-positive blood to Rh-negative recipients. Also, we have had reports of emergency departments having to close for admissions due to low blood availability.

A sudden, dramatic reduction or elimination of Euroblood will worsen these medical issues and have a catastrophic impact on the delivery of hospital care in our area. Replacement of this resource with our own collections is our long-term goal. It cannot be achieved, however, abruptly or without substantial planning and investments. Rapid replacement from other sources is also not realistic given current global blood shortages. Therefore, any new policy that eliminates Euroblood will in effect reduce the availability of blood to our hospitals by 25 percent or, put another way, approximately 1.5 to 2 percent of the nation's supply. We feel it safe to say that this magnitude of blood shortage will likely produce increase in hospital mortality in our area.

We are very concerned about the safety of the blood supply. We support all regulations that have a clear impact on blood safety. However, we believe there must be a balance between any theoretical risk and the measurable risk of a deficient blood supply. We respectfully request that in making your recommendations you take into account the consequences of any action that would cause either' additional donor deferrals in our area or sudden elimination of the Euroblood program.

Thank you again for this opportunity, and I welcome questions if you have any.

DR. FREAS: Thank you, Dr. Jones. Our next speaker will be Mr. Chris Healey, President of the ABRA, a trade association for setting standards for the plasma industry.

MR. HEALEY: Good morning, and thank you for the opportunity to address the committee. I have just a few brief comments.

ABRA is the trade association and standard setting organization for the producers of plasma for further fractionation. ABRA members include approximately 380 community-based collection centers across the U.S. that produce roughly 11 million liters of plasma for fractionation in the U.S. and Europe. Plasma donors are valued members of a society whose donations provide the raw material for a wide area of life-saving and life-sustaining

products.

Assuring an adequate and healthy donor base is one of the industry's primary goals. Over the last decade great strides in plasma safety have been made through effective regulatory policies, such as those set by this body, and industry imposed safety and quality standards. As a result of industry standards and government policies, plasma therapeutics are safer today than ever before.

Despite these safety gains, industry recognizes the need to remain vigilant about potential health risks from emerging and newly identified pathogens. As a result, the plasma industry approaches the vCJD problem as though the risk were real today. This is why we have taken a number of steps to further assure the safety. For example, we agree with regulatory authorities to withdraw products derived from plasma of vCJD donors, while we defer donors who have spend considerable time in the U.K. while we perform studies to evaluate partitioning of prions and fractionation steps, while we prepare studies to investigate prion infectivity in vCJD blood and plasma, and while our members invest in the development of improved methods for prion testing.

Further, ABRA, along with its partner association PPTA, has established expert working groups to address TSE risks. These working groups provide a venue for information and research exchange among industry members. They also

serve a key liaison function with regulatory authorities to assist in the science-based decision-making that must accompany decision-making with regard to vCJD risks. Finally, they produce materials to educate consumers about the current state of knowledge regarding vCJD risks.

As noted, assuring the adequacy and safety of plasma is one of our primary objectives. For this reason, we ask that you carefully consider any policy that might negatively impact the current donor base. Notwithstanding this, the plasma industry stands ready to take whatever steps are necessary to minimize the still theoretical risk associated with vCJD. Thanks.

DR. FREAS: Thank you, Mr. Healey. Our next speaker will be Dr. Merlyn Sayers, for the American Blood Centers. Dr. Sayers?

DR. SAYERS: Thanks, Dr. Freas. I would like to just read this brief statement into the record on behalf of America's Blood Centers. America's Blood Centers, or ABC, represents 75 not-for-profit community independent blood programs that together account for something like 50 percent of the nation's volunteer donor supply.

ABC appreciates the fact that the FDA has, as a result of regular meetings of this committee, encouraged frequent review of the emerging information about bovine spongiform encephalopathies and other encephalopathies as

well. Against the background that there still is no evidence to demonstrate that new vCJD is more than a theoretical risk for human blood transfusion recipients, ABC also appreciates FDA's commitment to requesting review of previous restrictions on donors for their continuing appropriateness. At the same time, however, ABC recognizes that the spread of bovine spongiform encephalopathy to other European countries must prompt debate about possible modifications of the recent deferral criteria that apply to donors previously visiting the U.K.

In considering any need for additional precautionary measures, ABC asks the committee to balance new restrictions on donation against continuing deferral of donors. ABC recognizes that transfusion safety, which is of paramount importance, is a goal that must be linked to blood availability at a time when blood shortages are nearly chronic in nature and increasingly result in the cancellation of non-urgent surgeries.

That concludes my statement on behalf of ABC. I would like a couple of sentences, Bill, on behalf of my own blood program. I am taking off my ABC hat here. There is one group of blood donors that we have ignored in these considerations. It used to be that blood donation was a volunteer activity involved in the release of one pint of blood. Things have changed and their levels of altruism that

individuals express in their participation in blood programs. Apheresis donors, platelet apheresis donors are a particularly committed group. They are different in that they are prepared to donate something like two hours of their time to the procedure.

These are a different batch of individuals, and some of them have the characteristics that have been pointed out earlier. They are an older group of people, quite often more educated, quite often from a different socioeconomic group. In our own experience in a large community blood program in Dallas, these are the folks that have most frequently traveled. Our loss of these individuals to any new restrictions will be quite devastating, and I would like the committee to bear in mind that it is not just whole blood donors that we are concerned about the loss of, but we are also concerned about a very important group, the platelet apheresis donors as well. Thanks, Dr. Freas.

DR. FREAS: Thank you, Dr. Sayers. Our next speaker is Dr. Rebecca Haley, speaking on behalf of the American Red Cross.

DR. FREDERICK: Thank you. I would like to thank the committee for this opportunity to address this group on an important safety issue. I am Jackie Frederick, the Executive Vice President for Biomedical Services at the American Red Cross. The American Red Cross provides almost

half of the blood needed in this country to patients and hospitals worldwide.

The safety of the blood supply is paramount and is the Red Cross's number one priority. The Red Cross and the Food and Drug Administration believe it was a prudent step to ensure blood safety by deferring blood donors who have traveled to or lived in the United Kingdom based on the theoretical risk of vCJD and the lack of a blood screening test.

The current deferral is for people who have traveled to or resided in the United Kingdom for six months or more between 1980 and 1996. The American Red Cross supports expanding this deferral to include France, as well as western Europe given the growing evidence of BSE in those countries.

We believe the TSE committee should consider a further tightening of the deferral period to less than six months in the U.K. We also believe the committee should examine extending the exposure period between 1980 to the present instead of the current deferral between 1980 and 1996.

There is evidence in animal models that TSE is transmissible through blood. We must be cautious to ensure the safety of America's blood supply for vulnerable patients. The American Red Cross calls for expanded research

to better understand the TSE pathogen and to create a TSE-specific blood screening test. We believe that if this is done in the next two to three years we will have a means to assess the true risk which will better inform our donor selection criteria.

We estimate that expanding the deferral criteria would reduce the current number of American Red Cross blood donors in the range of approximately 6 percent or an additional 4 percent. Therefore, it is our shared obligation to embark on a sustained national campaign to educate the public to increase the number of Americans who donate blood.

The one thing we can control during this time is blood availability. Only 5 percent of Americans donate blood. Recently, in the past year, the American Red Cross instituted the U.K. deferral which resulted in potentially a 2 percent donor loss, and implemented new screening methodologies for donors for hemoglobin determination, which resulted in an immediate 6 percent loss of our donor base. But I am proud to say that today we are collecting 3 percent more blood than we did last year. So, clearly, the American public will respond to the availability issue, and it is an issue that we can control.

The American Red Cross knows it will take a major investment of time, money and resources to attract new donors and retain current donors to meet the increasing

needs of patients nationwide. We are prepared to take on this public responsibility along with others who share our mission to ensure a safe and available blood supply. The Red Cross is prepared to implement tightened donor criteria across our nationwide system. Thank you.

DR. FREAS: Thank you very much. Our next speaker is Dave Cavanaugh, from the Committee of Ten Thousand, an advocacy group for persons with HIV and AIDS.

MR. CAVANAUGH: The Committee of Ten Thousand represents people with hemophilia who contracted HIV from the blood supply -- their medicine, if you will -- in the 1980's, and we are very pleased to acknowledge that Congress finally passed appropriations for relief payments to these families, just last month, 1999 after the injuries occurred in '82 to '87.

On the question before us, I would definitely encourage the committee to take the most conservative line possible with a disease of such unknown characteristics and newly emerging sources. Please be wary of arguments in favor of protecting the supply at the expense of exploring some of the possible true safety issues. Supply can be affected through campaigns, through presidential announcements which have been too rare, and many other means. I know it is difficult but it can be done, and it doesn't have to be done through merely compromising the quality of the product.

There are people here who are still calling the risk of CJD transmission through blood supply theoretical, and I think the more we are hearing of risk at each meeting through the elapsing of longer incubation times, more and more systems that are coming on line in various countries, and the clinical data that we are finding leading to some cases that have been found and remain open files without cause identified, it would be only prudent to rescind that label for now and remain open to examining the different sources. For example, last summer at the meeting we had presentations from representatives from various countries, like today, except that Portugal was not represented on the panel and they have a very high rate. I did a bit of searching of the Portuguese press and found a number of things that were quite disturbing -- 10 BSE-related deaths every month. The head of the national veterinary surgeons organizations says food control in Portugal is inefficient. The union leader for meat inspectors says inspection of food products is non-existent. The conclusion of the veterinarians is that Portuguese beef is unsafe.

We have the FDA, a matter of a week or two ago, finding that beef processing in this country is not observing some of the requirements on it. We have evidence on the CWD coming out, chronic wasting disease, in animals in this country, and we cannot expect those who eat beef in

this country not to donate blood, but there are a number of sources of transmission of this infection into the blood supply which I hope the committee will heed in realizing that the countries of Europe and those otherwise constituting as second wave of the U.K. epidemic pose a threat to America's blood users. Thank you.

DR. FREAS: Thank you, Mr. Cavanaugh. Is'there anyone else in the audience who at this time would like to address and make brief comments before the committee? I see no one, therefore, I turn the microphone over to Dr. Brown.

Committee Discussion

DR. BROWN: There are nine questions before lunch, each of which, the FDA tells me, requires a vote. What I would like to do, with the committee's approval, therefore, is change the format just a little bit and actually save the discussion for each question. Therefore, what I would like to do is pose the question, have a discussion if there is one, and then have a vote. Because of the number of votes, not only this morning but during the rest of the two days, we will not have any explanatory commentary associated with vbting. We are going to do it like the U.S. Congress and simply vote through.

The questions are going to be put on the screen, and they are in Topic 1. The first question is, are recent data on prevalence of vCJD in the U.K. or the potential risk

of transmitting vCJD by human blood or plasma sufficient to warrant a change in current FDA policies regarding deferrals of blood and plasma donors based on a history of travel or residence in the U.K.?

So, the first question relates strictly and uniquely to the United Kingdom, and it is simply a reassessment of the what the committee had recommended in its previous meetings. Is there sufficient data to warrant a change? That question is now open for discussion. Ray?

DR. ROOS: One of the speakers mentioned the possibility of changing from six months to three months. We have figures on six months, at least the prediction was an 86 percent person day decrease in theoretical risk with 2.2 percent increased number deferral of donors, and I want to know what those figures would be actually for three months.

DR. BROWN: Allan? This is probably only you first reappearance. Do you want to put anything on the screen? I think you had it on one or two slides. If you have it in your head we don't need the slide.

DR. WILLIAMS: The first slide I presented was the analysis for the current U.K. deferral, 2.2 percent loss. Given a deferral of three months with the six-month deferral already in place, not de novo -- in fact, if you want to look at the three-month de novo a year ago and what the impact would be, that is at the end of your handout -- but

given a change to three months with the six months in place, the residual risk removed is 21.2 percent. Considering the European picture, the total theoretical risk removed is 77.5 percent. Additional donor loss above and beyond the six months is 1.2 percent. The percent residual removed, compared to a 1 percent donor loss, is 17.6.

DR. BROWN: Allan, let me clear this up. First of all, these are figures just for the U.K., not for Europe.

DR. WILLIAMS: This is only the U.K.

DR. BROWN: So, three months instead of or on top of -- 1 don't know what you mean by on top of six months.

DR. WILLIAMS: Six months is already in place; if you change that to three months.

DR. BROWN: So, the six months is what percent loss?

DR. WILLIAMS: On top of the six months it is 1.2 percent.

DR. BROWN: So, I.2 plus 2.2? That is 3.4.

DR. WILLIAMS: I think it might be easier -- instead of trying to turn the incremental analysis around, let's look at the three months by itself, which is at the end of your handout. It is U.K. three months considered by itself without consideration of what is already in place. The U.K. risk removed is 93.3 percent instead of 86 percent. That is what you are looking for. The donor loss is 3.4

percent.

DR. BROWN: That is what you wanted, wasn't it, Ray?

DR. ROOS: Yes.

DR. BROWN: Roughly 3.5 percent donor loss and the risk removal was what, Allan?

DR. WILLIAMS: It was 93.3.

DR. BROWN: Against the present?

DR. WILLIAMS: Against the present 86 of U.K. risk.

DR. BROWN: And you pick up a few percent and you lose a little better than one percent more donors than are currently lost. Other discussion? Other questions? Yes?

DR. GAYLOR: I have quite a concern about the estimates based on the Red Cross 1999 donor travel survey. A 50 percent response rate to a survey is not good; 50 percent of your population is unknown to you. You recognize that there is more travel among the higher age people, more educated people, presumably with higher economic status. Quite possibly these are the people that are also responding to the survey. There tends to be a higher response rate among the higher educated, older people. I suspect you are overestimating the amount of travel in your donor population. It might just be a small overestimate; it might be substantial. So, I think we are dealing with quite possibly overestimates of what the impact of the deferral

is.

Typically, when you have such a large population of non-responders in a survey, as you follow up the non-responders, not with a mail survey but with a telephone survey, maybe a small percent of them, only five percent of the non-responders, and determine if the non-responder population is like the responder population in order to really estimate what is going on here. So, you know, there is nothing one can do about that today but something that is important in the decisions that are going to be based on a survey should also include some follow-up of the non-responders.

So, I would take all of these calculations with a grain of salt. You know, we will do the best we can. We have to assume non-responders are like responders, but this is not typically what happens in surveys.

DR. BROWN: Thanks. We have a habit of using a lot of salt in our deliberations. Do you want to respond?

DR. WILLIAMS: I agree with the comment, and I think I alluded to that problem when I said that the education and the age factors were higher. One thing I didn't mention is that this is an anonymous mail survey so secondary validation measures weren't possible for this. We would have liked to have had more than 50 percent but you get what you get and we were on a short time frame. So I

acknowledge the comments that it is a possibility that we are over-calling the travel risk.

DR. BROWN: Stan?

DR. PRUSINER: It seems to me, with respect to the first question about the U.K., we have several issues that we really should address. One is how good is this 2.2 percent number because now we have 8 months that have gone by? Was the estimate that you gave us -- how does that match what we really know in terms of loss? Because that, I think, impacts these decisions which are really guesses.

DR. BROWN: Well, bear in mind the talk that Paul McCurdy gave. After this was all in place, it was a flat-line supply. So, even if it is not 2.2 percent, whatever percent it was, was being met.

DR. PRUSINER: I understand that. I agree. I think this is very important. So, the theoretical increase if we take it to three months of 1.2 percent, a 3.4 percent loss may not be a 3.4 percent loss at all if we think that Paul McCurdy's data is correct. So, I think this is a very important issue to discuss. I am not sure what conclusions to come to.

The second issue is that I am not sure still that 1996 is the right cut-off time. It may be that we should be taking it to the present. The problem for me with the U.K. data on BSE incidence is that those graphs showing the

decline on BSE are based upon the clinical diagnosis and confirmed pathology of BSE cases in the U.K. What we are seeing in other parts of Europe is that a large number of the cases that are now being reported are being reported as BSE positive cases in animals without symptoms. So, we kind of have apples and oranges here, and we have a false sense, I think, of the decline approaching zero in the U.K. where the numbers are still much higher than in any other part of Europe. So, I am not totally convinced that we should just say, okay, 1996 is the right date.

DR. BROWN: Yes, one other comment about that and that is that, while that may be true in the United Kingdom, the measures taken to prevent the introduction of even a potentially infected cow exceed by far those of virtually any other European country. So, even if there were more cows than we think that were infected with BSE, my guess is that probably British beef at the moment is about the safest beef in the world.

DR. PRUSINER: Well, we would have a dispute over that, Paul.

DR. BROWN: No! Don?

DR. BURKE: It seems that we are getting ahead of ourselves here in asking questions about the impact on the blood supply, but the specific question is are the recent data on the prevalence of the change in vCJD or the

potential risk of transmitting vCJD by blood sufficient to make a change? And, I think we should address ourselves to that right now.

I will summarize my own impression of the presentations so far, and that is that I think there is a difference in interpretations of the prevalence of vCJD and, if anything, it is at the upper boundary of the epidemic. Since we made this recommendation the estimates for the upper boundary of the epidemic in humans has been dropped. So, if anything, the worst case scenario in the U.K. doesn't look as bad as it did when we mad the recommendation in the first place.

The second item that we are to discuss is are there any new data with regard to the risk of transmission by blood, and I think the answer to that one is no. I have not seen any one way or the other, and I am open to additional presentations, if there are some.

DR. BROWN: Well, the only "con" piece of data that has been published since our last deliberation is the incubation period, the presumed transmission of BSE from an incubation period sheep to another sheep. That, I think, does not fundamentally change our way of thinking but it is one more little piece of evidence in the direction that, yes, at least under experimental circumstances, blood can be shown to be infectious. Again, all that assuming that that

transmission is a true transmission.

DR. PRUSINER: I think the big difference between two years ago and now or a year and a half ago is that if one looks at the number of vCJD cases by year -- and Paul Brown presented Bob Will's data -- I think it is really dramatically different. In 1996, including the few cases retrospectively in 1995, there were 10, 12 cases of vCJD. In the next year, 1997, there were about 12. Then it jumped to 17 in 1998. Then it dropped back to 12 in 1999 and everybody thought, well, you know, this is the variation, that it bounces around. Now we see about 30 cases for the year 2000. It seems to me that we don't know where this curve is going to go. We don't know whether next year the number will be 15, in which case it will be part of this fluctuation and all of these very conservative estimates are reasonable. If the number goes to 60 next year, so it is a doubling, then we have a very different view of how this is going to go and we are really not going to know for the next few years. So, I don't really think that we can believe for a moment that we have an understanding that this process is going to be not as big as we once-thought, and all of these estimates are made on too little data.

DR. BROWN: Still, with every year that goes by there is more data, and what we have seen is that the data that has accumulated, granted the rising slope of new vCJD

in the British Isles is, in fact, less steep than it was originally thought, and the more data that comes through each year, the lower the upper limit of the eventual number of cases. Granted, modeling isn't perfect, for sure, but, of course, we don't know exactly what is going to happen. We are not soothsayers. But I would suggest also that the rise in vCJD that has occurred has actually led to models or modeling in which the ultimate outcome is less severe than was originally modeled. Ray?

DR. ROOS: I just want to return to the issue of recent data about transmission from blood. Although there is an N of 1, near as I could figure out, that is, there was a blood transfusion that took, nevertheless, I have to pay attention to that data as being potentially troubling because it was a subclinical animal, as I understand it, and because it did transmit by the peripheral route, by blood transfusion. So, I do think that is recent data that certainly gets one's attention at this point.

It might be of concern with respect to the whole modeling that one has at this point which I think, in a way, doesn't deal with the possibility that one could get amplification in human to human transmission. We have no data at the moment that that has occurred but, of course, we only have human cases for the last six years. If that were to occur we might see a lot more unsuspectingly vCJD. The

fact that we do have this N equals 1 transmission gets my attention and the concern that one should consider the possibility of being more stringent with respect to U.K. residents and the limits of it if the downside isn't too much of a penalty.

What I see with respect 'to the downside is that although there may be an increased number of donors that are deferred, nevertheless, blood banks and Red Cross have responded and they were able to recoup that decrease. So, I suspect that the predictions with respect to increased deferment might occur but I also wonder whether we will just still have a flat line with respect to supply because of increased energies to get the blood in other ways.

DR. BROWN: Pedro?

DR. PICCARDO: Regarding the estimates, we have to consider that of the uncertainties that we have so far only the methionine homozygotes developed the disease. So, in this box of uncertainty we have to consider that it is very possible that people who have these zygotes will develop the disease. So this adds to the uncertainty. I think we have to keep that in mind.

DR. BROWN: Yes, that is an interesting point. On the other hand,, it is possible that a human adapted DSE, that is a primary CJD in the event of a transmission might not just transmit to met/met. We just don't know but I don't

think we can assume that because primary transmission from a cow to a human has to date only affected the methionine homozygotes that a secondary infection might not be indiscriminate.

DR. PICCARDO: Right. My point is that we probably have to be open to the possibility --

DR. BROWN: Sure, exactly. Go ahead.

MS. FISHER: Public confidence in the safety of the blood supply is of paramount importance, and the American Red Cross, I think, is arguing for the precautionary principle to be employed, and I think as the primary supplier of blood to Americans -- as a consumer I am very persuaded to heed the implications of theoretical risk and the limitations in screening technology, and I believe that the committee needs to take very seriously the position of the American Red Cross arguing for a change.

DR. BROWN: I would, in contrast, hope that the committee paid absolutely no attention to the American Red Cross recommendation and made a completely independent decision. Yes?

DR. NELSON:. To me, somehow the idea that lowering the cut-off to three months has less of an effect than lowering it to six months is counter-intuitive. I would think that the shorter the time someone spent, that there be an incremental loss of donors.

DR. BROWN: That is right.

DR. NELSON: Between three and six months it is half the number of donor loss as six months and above, and I just wonder. To me, that is counter-intuitive. I think the shorter the period, you should probably exclude a larger number of donors and I wonder if somehow that relates to the incomplete responses.

DR. BROWN: I am not sure that you haven't misunderstood or perhaps I have misunderstood you. Allan, would you again put our committee member straight in case there was a misunderstanding?

DR. WILLIAMS: I suggest that in case there is a problem with the calculation of the three-month implemented on top of the six-month that you only consider the three-month as a stand-alone, in which case donor loss is 3.4 percent versus the cumulative six-month of 2.2 percent. Those are the figures that were considered before and I think do make conceptual sense.

DR. BROWN: In other words, what you intuit is, in fact, correct, that if you drop the deferral to everybody who has been at least three months you lose 3.5 percent of the donors. If you have a six-month deferral, that is they had to stay in the U.K. for at least six months, the donor loss is less because there are fewer people who stay in the U.K. that long. That is correct.

DR. NELSON: I would have thought that the shorter the interval, there would be an increasing number of donor losses.

DR. BROWN: There is. That is exactly what he said. Yes.

DR. PRUSINER: Paul, I think what he is saying is he would have thought that it might have gone to 5'percent or 6 percent.

DR. NELSON: That is exactly right.

DR. PRUSINER: That is what he is trying to say.

DR. NELSON: Yes, I realize that 3.4 is more than 2.2 but 2.2 versus 1.2 is the issue I am getting at.

DR. WILLIAMS: The greater than five-year interval goes all the way up to the 17-year period. So, you have people who have been over there for 10 and more years included in that larger group and it really weighs that initial cut.

DR. BELAY: I have a question for Dr. McCurdy.

DR. BROWN: He was just going to ask you something.

[Laughter]

DR. BELAY: I am still concerned about the supply issue and the impact of the U.K. donor deferral policy that has already been put in place. Now, you showed data through November, 2000 and we know that different blood centers were

implementing the policy at different times. So, do you believe there was sufficient time for full implementation of the policy to have exerted its effect so that you would pick it up in your data?

The second question is did you notice any regional differences in the supply, which may not actually show in the graph that you showed us?

DR. MCCURDY: I think that the requirement placed by the FDA asked all blood centers to implement the U.K. deferral by April, 2000. Many blood centers, perhaps close to half of the blood centers we sampled, implemented it before October, 1999. Some of them implemented fairly soon. So, I think that it is very hard to look at the graphs and say there is no blip here and, therefore, there is no change. I think the supply remained fairly constant over that period of time. So, I think probably the impact of implementing the procedure is reflected in those data, although not any individual blip.

You asked about regional differences, and we have relatively small samples from various different regions of the country, but we do have the data broken down by PHS regions and the northeast, Mid-Atlantic area from roughly Washington, Baltimore, north, suffered perhaps a little bit of a gradual decline in collections. The rest of the country was relatively constant or there was some increase over that

period of time. So, there was some difference by region. I didn't show that because each individual curve on the graph would have such a small N that I would worry about the significance of it.

DR. BROWN: I must remind you that if we continue the discussion we are not going to get to lunch until three in the afternoon, and as soon as possible I would like to put this question to rest. Go ahead.

DR. KATZ: We have seen the supply side of this and I think it needs to be on the record that that is less than half the question. The demand side of it is critically important. Demand for components is rising, depending upon where you are, approximately 5 percent per year. And, I think we have all heard reference to the increased seasonal shortages and appeals that have been required during the past year. So, critically important is that the committee considers this balance and that they understand that a flat supply does not address increasing demand.

DR. LURIE: I guess Don said we should be discussing (a) separately from (b), and (a) is about the prevalence. I actually disagree with that and I think the way the committee is talking about that reveals that it doesn't actually make that much sense to discuss them separately.

Really, the question is from either of these

sources of data, prevalence data or donor deferral data, do we, in sum, feel that there is justification for a change in FDA policy? One might feel yes to (a) and no to (b), or vice versa. So, I think really that ought to be combined and we should just discuss whether the totality of what the data show is sufficient to justify revisiting of the question.

DR. BROWN: My own opinion is that you are absolutely right, and that the (a) and (b) are on the table here and what we are being asked basically is, is the data sufficient to warrant a change. The data is obviously risk-benefit data. Question (a) is worded neutrally and question (b) is not. There is that little word "adverse" in question (b). But if we took the "adverse" out -- I mean, I don't frankly feel bound by the language, even though I passed on it.

DR. LURIE: It is improbable that donor deferral would have a positive effect on the blood supply.

DR. BROWN: Yes. I think (a) is asking whether or not there is evidence that warrants a change, not whether it should be more stringent or more relaxed. That is how I read question (a). All question (a) is asking for is a change. It doesn't stipulate whether it should be a change for the better or the worse. To that degree, it seems to me that what we are talking about is correct. We are really asking should there be a change. Probably the question should have

been does the committee consider that anything has happened since the last meeting to warrant a change, (a) and (b), and in what direction should the change go. Ray?

DR. ROOS: I think when we sat around the table a couple of years ago we didn't know what the impact of our recommendation would be.

DR. BROWN: Yes.

DR. ROOS: And now we have data about that, and then it came to time as to how much of a limit on residence time we would allow with respect to U.K. -- should it be one week or three months or six months, we did this predictive study and then we have some data at least to know what the impact is.

DR. BROWN: Another way to deal with this is to leave (a) and (b) in, but (a) is now just as such. (a) is being voted on as such and it is being voted on based on what we will loosely call the science -- has anything happened scientifically in the past year or two to warrant a change? Then, the second question deals with supply. So, the first question doesn't really have to do with the benefit or the adverse effect on benefit. The first question really has to do with risk, and is there anything that has happened in the past year or two that warrants a change in thinking about risk? That would be a decent question, and that is how I understand the question to have been worded. Yes?

DR. EWENSTEIN: If we look at it that way, and I agree with you, we are basically left I guess with three facts or sort of facts. One is the anecdote of the sheep, which I think is an experiment that is ongoing. Two is the lack of transmission in the human population, although there are very limited data that you presented. And, three is what I believe to be a much better looking curve on the'modeling but we can accept the fact that it is still very early on and perhaps needs another year to better define the curve. But, I do think that it is unlikely, especially from your presentation of Dr. Will's data, that the curve could possibly be as bad as we had thought it might be a year and a half ago.

With all those three together, it would be my own personal feeling that we should probably stay the course because none of those pieces of data that I see on the table are that compelling in either direction and they tend to almost neutralize each other.

DR. BROWN: I am putting the question as written, 1(a), to the vote. Ray?

DR. ROOS: I would say no.

DR. LEITMAN: Paul?

DR. BROWN: Yes?

DR. LEITMAN: I just wanted to make two points before you start the vote, based on what I heard this

morning. One has to do with donor availability. Families tend to donate together and spouses tend to both be donors. So, the elimination or deferral of a donor who comes to donate based on U.K. travel deferral often defers two subjects, the second of which never shows up. So, that is hidden in the fact that 0.8 percent is the actual written loss or documented loss as opposed to the slightly greater than 2 projected loss. I think it is exactly a 2 to 2.2 percent loss from our own institution.

My second point is kind of a difficult one to make perhaps to the consumer representative. An argument made by an industry supplier, commercial supplier such as the American Red Cross, of this nature may be made out of economic or political or with other strategies in mind that are not purely scientific and don't purely have the public health benefit in mind, which is why I most strongly support Dr. Brown's statement that the committee should be assessing the information presented here scientifically rather than on an industry recommendation.

DR. BROWN: I won't read your names. If you would just kind of tick your votes off, Dr. Freas will tally them up.

DR. DETWILER: Yes.

DR. EWENSTEIN: No.

DR. BURKE: No, there has not been sufficient

change to change the current course.

MS. FISHER: Yes.

DR. MCCURDY: No change.

DR. PICCARDO: No change.

DR. GAYLOR: No.

DR. NELSON: No.

DR. BOLTON: No.

DR. BROWN: No.

DR. BELAY: No.

DR. CLIVER: No.

DR. LEVIN: No.

DR. WILLIAMS: No.

DR. PRUSINER: Yes.

DR. BROWN: The question that is now before is ave the recommendations of the FDA concerning blood donor leferral, because of residence in the U.K. -- still talking tbout the U.K. -- had an adverse effect on the blood supply ufficient to consider a change? Discussion? I will put the uestion to a vote. Ray?

DR. ROOS: No.

DR. BROWN: Do you want me to start alternately very now and then to give you a break?

DR. ROOS: Please.

DR. DETWILER: No.

DR. EWENSTEIN: No.

DR. BURKE: No change.

MS. FISHER: No.

DR. MCCURDY: No.

DR. PICCARDO: No.

DR. GAYLOR: No.

DR. NELSON: No.

DR. BOLTON: No.

DR. BROWN: No.

DR. BALEY: No.

DR. CLIVER: No.

DR. LURIE: Yes.

DR. WILLIAMS: No.

DR. PRUSINER: No.

DR. FREAS: One yes vote, zero abstained and 15 no votes.

DR. FREAS: Unofficially I have two yes votes, no abstained votes and 14 no votes. The yes votes -- correct me if I am wrong -- are Dr. Detwiler, Ms. Fisher and Stan Prusiner. Correction, there were three yes votes, 13 no votes and zero abstained.

DR. BROWN: The question that is now before is have the recommendations of the FDA concerning blood donor deferral, because of residence in the U.K. -- still talking about the U.K. -- had an adverse effect on the blood supply sufficient to consider a change? Discussion? I will put the

uestion to a vote. Ray?

DR. ROOS: No.

DR. BROWN: Do you want me to start alternately very now and again to give you a break?

DR. ROOS: Please.

DR. BROWN: Linda?

DR. DETWILER: No.

DR. EWENSTEIN: No.

DR. BURKE: No change.

MS. FISHER: No.

DR. MCCURDY: No.

DR. PICCARDO: No.

DR. GAYLOR: No.

DR. NELSON: No.

DR. BOLTON: No.

DR. BROWN: No.

DR. BELAY: No.

DR. CLIVER: No.

DR. LURIE: Yes.

DR. WILLIAMS: No.

DR. PRUSINER: No.

DR. FREAS: One yes vote, zero abstained and 15 no votes.

DR. BROWN: Yes?

DR. KATZ: I am just interested, as a guest from

industry, in the yes vote on that question, a very brief reaction.

DR. LURIE: The reasons are that, in sum, the predicted decreases in the supply, best as we can tell, seem to have been overestimates and, at least if looked at from the supply side, we see the flat line. Your point about one has to look at demand as well is a well taken one, but the evidence, as I see it as presented to us today, suggests that there was an overestimate of the amount of impact on the blood supply.

DR. BROWN: The crucial word was "adverse." We will allow a vote change to a unanimous no vote.

Now we get into a little bit of uncharted territory, and we ask approximately the same questions anew with respect to France. Should the FDA recommend deferral of blood or plasma donations by persons with a history of travel or residence in France for an aggregate period of ten years or more after 1980?

Now, there are two points I want to emphasize here. One is the ten years versus six months, based on what you have heard about probabilities of exposure. The second is that it is open-ended. All right? It is 1980 to the present. Probably, rationally it might be 1985 to the present but 1980 is all right, and the reason for that simply is, as you have heard this morning, that the risk in

Europe probably had a lag period of several years relative to the risk in Great Britain, and continues. That is the point -- and continues and may possibly, in some countries, be worse next year than it is this year. We just don't know. So, those are two important points to bear in mind when we have this very brief discussion. Yes?

DR. EWENSTEIN: You know, this ratio of 20 to 1 which seemed to be based on the imported risk makes some sense, and it fits, as you pointed out, very roughly with the incidence of the human disease so far. This is probably what the committee should have voted on when it was considered last time, if we just wanted to be consistent. But what I think is more difficult now is the question of whether there is an endogenous risk, in which case this ratio of 20 to 1 in 10 years to 6 months doesn't make as much sense. And, I think that is the part that maybe other folks on the committee understand a little bit better. In terms of the imported risk these numbers are consistent and do make sense to me.

DR. BURKE: Although you use the number 20 to 1, we heard two other estimates of what the relative risk estimates were for France versus the U.K. We heard one from Dr. Giulivi of about 100 to 1, as I understood it, and we heard one from Dr. Williams of 10 to 1 in their estimates, as I understood it. It might be useful if we had a defense

of those. My guess is they are indefensible.

DR. BROWN: Yes, and don't overlook the fact that the committee is certainly within its responsibilities to say we couldn't make a recommendation, with respect to a given time, without more information about just what you said. That is, I know the question is phrased in such a way that it says 10 years from 1980 to the present. We have every possibility in saying no to that but yes to something that is either vaguer or requires a little more work on the part of the people who are data suppliers.

DR. BURKE: Again, as I understood it, our Canadian colleagues did make a recommendation that was different than this. They have the six-month block as well. Is that correct?

DR. BROWN: Yes, I think that must have been strongly influenced as well by the fact -- maybe I am wrong. Tony, was that influenced a good deal by Quebec as well?

DR. GIULIVI: That 100 to 1 is a traveler, a Canadian traveler to France coming back, but the endogenous risk, you know, of importing foods from U.K. to France is still 1 in 10. So, that still stays the same. It is how many people in Canada went to France on a national level, and that is the risk.

DR. BROWN: You are including Quebec travelers?

DR. GIULIVI: Quebec travelers, yes. Dr. Belay?

DR. BELAY: What percentage of the blood supply in the United States will be impacted by a ten years residence in France?

DR. BROWN: That, I guess, Allan, is something that you didn't have a figure on, or perhaps you did? Were your figures based on six-month combined U.K., or was it ten years France, six months U.K.?

DR. WILLIAMS: I didn't present data specific to France because of the way the survey was constructed. We had intervals for travel to Europe and total prevalence for visits to France.

DR. BROWN: So, U.K., France was whatever period was sliced on the chart. That is, travel to the U.K. or France for such-and-such a period.

DR. WILLIAMS: Right.

DR. BROWN: Okay. The other practical issue on this is what do you do if someone tells you they were in Yugoslavia for five weeks, France for eight and a half years and the U.K. for two months? Does that add up to a deferral? That is a heavy piece of arithmetic for the question askers.

DR. PRUSINER: That is question number four.

DR. BROWN: Oh, it is? I have anticipated something. So, we are still back on 2(a).

DR. BELAY: Dr. Brown, I would still like to have an estimate or a guesstimate, if you will, based on the

survey conducted by the American Red Cross. What would be your guesstimate for the ten-year period in France based on the data that you collected?

DR. BROWN: Do you have any idea, Allan, what that might be?

DR. WILLIAMS: The curve for the U.K. deferrals for one year goes out to 1.5 percent and gradually decays from there. I don't have the information for that five-year data point but I believe it is around 0.5 percent. So, if you use that correction factor for France, 0.7 times 0.5 percent, one could guesstimate perhaps around 0.3 for that time period.

DR. BROWN: My sense of one of the reasons the committee didn't mess with France the last time is that, yes, it would be logical and consistent, and if it were deferral based on ten years, given a 1 to 20 relationship, which would be a logical one, the yield of Americans who spend ten years in France would probably be so small it wouldn't be worth asking the question. Ray?

DR. ROOS: Well, I guess what has changed over the last six months are some perceptual aspects with respect to France and BSE, which I think are worth noting. The BSE cases are relatively small but this grocery store incident, although it is an incident, brings home the realization that infected BSE material may not enter into the human food

chain and that is certainly concerning. So, although the BSE outbreaks are small still, we are not quite sure as to contamination of human food and how often that might have occurred over the number of years that BSE has occurred in France.

DR. BROWN: Yes, this again boils down to such an easy decision, one, all the things we don't know -- we don't know the risk in France for a traveler, over what period of time. We don't know if someone is exposed if they are going to get infected. We don't know if they are infected, if they are going to have blood that is infectious. And, we don't know if the blood that is infectious is going to transmit to disease. So, we should be able to make a decision.

[Laughter]

DR. EWENSTEIN: All that aside, another piece of data that we hadn't discussed that was in our information packet is the paper that came out, I think it was in Nature late in 2000, on the sort of gearing ratio between cow and human infection, and it appeared to be about --

DR. BROWN: I am sorry, what ratio?

DR. EWENSTEIN: Sort of a gearing ratio, in other words, how many people would be infected, based on the U.K. epidemic, from a single cow. And, we had talked about thousands of people potentially from a cow and the new numbers seemed to be more like two, again, based on

modeling. If that is true, then the absolute number of infected cows in the country would have a tremendous impact. For example, in France, although the numbers are increasing the absolute numbers are still very small. So, if you look at the maximum people at risk of every one of the 100 infected cows, you know, transmitted to two individuals would still be very different than our worst estimates. So, with that in mind, I think the question is that we have a period in time when the risk was from the U.K. beef and now we have a period in time when we are not sure what the epidemic in the cattle is, and it is very hard to come up with a recommendation for total number of years based on two very disparate risk factors. I mean, I am not sure if everyone is agreeing with this analysis --

DR. BROWN: Yes, and that is also true for the whole of Europe. That is to say, anything that is going on in Europe now is certainly endogenous. It may have originated as contaminated feed infecting cattle in Italy or Austria or France but now it is almost certainly the result of having recycled that original material into French-born cattle or Austrian-born cattle, or whatever.

DR. EWENSTEIN: Right, but what I mean was there was an actual risk of U.K. beef exposure --

DR. BROWN: That is right.

DR. EWENSTEIN: -- and now we are talking about

the reintroduction or the introduction of infection --

DR. BROWN: That is right, yes.

DR. EWENSTEIN: So, I think the ten-year period makes sense based on what I am calling exogenous risk for France, and what is harder for us to calculate now -- and this is going to be true for all the BSE countries -- is the new emerging endogenous risk and this is where I would agree with the open-endedness and certainly not using '96 as a cut-off. That makes no sense for the countries in which BSE infection may be just emerging.

The question is can we use ten years as a reasonable number for now? It seems like a reasonable compromise, recognizing that we don't know how rapidly the number of new BSE cases will go up in these countries but what we say about France should be consistent with what we are going to say later on, in the next question, about the other BSE-infected countries. And, I think that is going to have to be deferred until we know more about those epidemics. So, I think for now the ten years, the open-endedness, makes sense for France based on the prior risk data that we have.

DR. BROWN: It really boils down to whether the committee would like to take a very, very conservative position in the presence of ignorance, for the time being, or a more liberal position, saying either way we really

don't know what the situation is yet. Probably in a year, six months to a year, the whole BSE situation in Europe will be vastly clarified. So, in the interim do we want to add more deferral for the sake of prudence and the possibility that Europe may explode, or think that we really should stay at status quo until we find out. Yes?

DR. LURIE: I agree with what Dr. Ewenstein was saying and in other respect comments put the focus back on the cows and less on the people, and there only are three cases in France, which is the primary reason we are focusing on France. But, I have brought along a slide from Dr. DeCrow's presentation earlier, one of our earlier meetings, which looked at the rates of infected cows per million cattle over the age of two, by country. I went over this at a previous meeting where I previously argued on my own for an extension of a ban beyond Britain. The U.K. rate was 422 per million cattle. The Portuguese rate in 1999 was 236 per million cattle; Switzerland, 53; Ireland, 27; and everybody else, including France, was in the single digits. Now, those numbers have changed since then and I don't know what the rates are because they weren't presented to us today. I would have personally found that very helpful.

But, I think that particularly when the number of human cases is as low as it is, I find the cow cases, whatever their limitations and there certainly are based on

the degree of active case finding that one engages in -- I find that very important, and that makes me feel that we need to focus on those, and I mention Portugal in particular.

DR. BOLTON: My concern with regard to France and other countries is that a 20-fold ratio I think seems to hold for the exogenous risk up to, say, 1996 or '98, but it is not clear to me that that holds at the present or in the future. So, six months in France in the last year or two may be a much higher risk than ten years from '85 to '95.

DR. BROWN: Is there any sense that the committee would like to answer that question without stipulating a time, and just answer the question without the time? Jean-Philippe would like to say something. Come.

DR. DESLYS: I am not on the committee but there is a difference between before '96 and after '96. The observation that it was transmissible to man changed many things and, notably on the reality on the ban of offals. So, the fact that it has been really applied and that it couldn't enter anymore, or not in such proportion, into human food has changed many things.

DR. BOLTON: But that sort of relies on at least the possible face of an increasing epidemic curve of BSE in France. You are relying on new regulations to prevent contaminated beef or beef products entering the food chain.

DR. BURKE: Again, my understanding in the U.K. is that there are no cows over the age three that go into the human food supply now. Is that a correct statement?

DR. BROWN: Yes, I think it is over the age of 30 months, and throughout Europe shortly no cow over the age of 30 months is going to get anywhere without a brain exam.

DR. BURKE: Right, the point being that there may be infected cows in those areas but there will not be cows ingested which are older than 30 months, whereas in the U.K. during the height of the epidemic that was not the case, and it was a very different ratio of the risk to humans during the height of the epidemic in the U.K. than it would be in the future where there is a limitation on the age at which animals can be eaten. So, even there I am not sure you can apply a formula that allows you to extrapolate into the future about what the human risk will be based on the cow formula. I would like to be able to do that and it is probably the best number we have but a direct extrapolation can't be done.

DR. LURIE: I didn't actually do that. All I did was I spoke to the point prevalence in 1999. I didn't make any comparison back to a previous point. Your point is well taken but it isn't what I said.

DR. BURKE: Okay. That would be the logic that would have extended the argument.

DR. BROWN: Dr. Cliver?

DR. CLIVER: There were actually three measures in he U.K. I don't know to what extent they are going to be mplemented in Continental Europe but the specified bovine ffals, the 30-month ban and incidentally the beef on the one ban were all measures that meant that just counting ick cows or possibly BSE-positive cows is going to be a not ery appropriate way of assessing risk for a while to come.

DR. BROWN: Dr. Belay and then we will vote.

DR. BELAY: In terms of specifying time, I think what we are doing is a balancing act, the risk on one side and also the impact on the blood supply on the other hand. So, I believe certainly a ten-year period would have less of an impact on blood supply than, for example, six months in France. So, I suggest voting on the question the way FDA has actually phrased it because of the possible impact on the blood supply.

DR. BROWN: Okay, let's do it. Let's start the other way around. Stan? We are voting on question (a) as it is written, should the FDA recommend deferral of blood or plasma donations.by persons with a history of travel or residence in France for an aggregate period of ten years or more after 1980?

DR. PRUSINER: No.

DR. WILLIAMS: No.

DR. LURIE: Yes.

DR. CLIVER: No.

DR. BELAY: Yes.

DR. BROWN: No.

DR. BOLTON: Yes.

DR. NELSON: Yes.

DR. GAYLOR: Yes.

DR. PICCARDO: No.

DR. MCCURDY: Yes.

MS. FISHER: Yes.

DR. BURKE: No.

DR. EWENSTEIN: Yes.

DR. DETWILER: Yes.

DR. ROOS: Yes.

DR. FREAS: I have six no votes. I have 10 yes votes and zero abstained.

DR. BROWN: That moots part (b). So, good for us! Other BSE countries, should the FDA recommend deferral of blood or plasma donation from persons with a history of travel or residence in other countries identified by the USDA as having BSE in cattle for an aggregate period of ten years or more after 1980? An identical question to question 2(a) but now we are talking about all other European countries. Dr. Cliver?

DR. CLIVER: I hadn't known until we got our

folders today about the Euroblood program. Obviously, the way we are going, if we are collecting blood even at FDA licensed centers in Europe, in'the countries that were mentioned, these are people who live there so that whole program is history. I think, one, we need to consider that in the specific context that was presented but, beyond that, it is hard for me to believe that even though New York City's blood supply is the only one mentioned here we are actually operating three blood centers in Europe for the sole benefit of the New York Metropolitan area. So, I think we need to know a little bit more about the impact of obliterating the Euroblood program that is beyond what we heard about the impact in New York City. We can't defer people for staying some period of time in these other BSE countries without obliterating the Euroblood program totally.

DR. BROWN: Yes, assuming that the FDA took that advice and issued that guidance, and assuming that the Euroblood program followed suit. That is, I could imagine that the Euroblood program is not bound legally to do what the FDA asks -- I think.

DR. CLIVER: Oh, I am sure that is true but, all the same, what blood supplier in this country would import blood against the recommendations of this committee, at the risk of whatever publicity would result?

DR. BROWN: We have the representative here. Maybe ıe could answer that question.

DR. CLIVER: But my question is not what is this going to do to New York. We have already heard that. The question is how many other blood supply areas of the United States are subscribing to the Euroblood program in addition › the New York Metropolitan area

DR. BROW-N: Anybody have an answer to that question?

DR. KATZ: Yes, essentially none. Euroblood is eculiar to New York, and developed out of differences in ransfusion practices between Europe and the United States hen, unlike here where plasma is a byproduct, in Europe the ed cells were a byproduct of their practices and it was a ood source of high quality product for New York. But they ıre the only ones in our industry right now who are ependent.

DR. BROWN: So, is it your thought, assuming is 'es, we will defer Europe, France, that the Euroblood ›rogram in New York City could function apart from that?

DR. KATZ: No.

DR. BROWN: No.

DR. KATZ: No, it would be gone.

DR. BELAY: What is the feasibility of gradually phasing out --

DR. KATZ: Phasing out Euroblood is in the strategic plan. I am speaking for New York Blood Center to a certain degree here. That is in their plan. They are actively trying to do that. It brings up a point I was going to make at some point in summary, that much of what we are talking about that is difficult with these issues could be taken care of if we had the right kind of top-down approach to blood donor recruitment that we think we need. That is, the highest levels of the government making this a high priority, which was going to lead me to request that the committee ask FDA to discuss this with the new administration as a very, very high priority but we get ahead of ourselves, I guess.

DR. BROWN: Yes, Linda?

DR. DETWILER: I just want to point out for the committee that the point about the specified risk material ban is a very important one, I think, when you are talking about the remainder of the Continent because not all the countries in the European Union had in place SRM ban and that went into effect just this past October, and that would be taking these high risk tissues out of the food and feed chains. So, that went European Union-wide just this past October, 2000.

DR. BROWN: One of the things we have to remember is that there is the future and there is the past. In the

future things are probably going to be quite a lot better but there are a lot of people walking around now which is what we are talking about, 1980 to the present.

DR. MCCURDY: I have a couple of comments and a question or two. One is whether the American Red Cross, who pushed for this type of change or an even more stringent one, is prepared to replace that 25 percent of the New York Blood Center's supply by collecting it and shipping it into New York from their blood centers around the country.

A second comment is that at one time, that is in the '70's and '80's, the Washington, DC Red Cross Blood Center, which has now merged with Baltimore, was importing about 100 units of red cell products a week from the New York blood program, most of which came to Europe. I guess I would assume from the comments that this is no longer the case, but I think this needs to be verified.

The other comment is that on several occasions publicly -- I am not quite sure on which of the advisory committees it was done, but on several occasions publicly I offered the Red Cross to be a broker for high level participation in. the blood program in the government, particularly in the Washington, DC area, but with the idea that this would ultimately be exported throughout the country and would not be restricted to the Red Cross as the blood collection in the country is not restricted to the Red

cross. Although there was very limited discussion of this ffer, nothing ever came of it.

DR. NELSON: I am trying to remember the resentation by the military, but it would seem to me that xtending this ban to ten years in Europe could have a evastating effect. I have forgotten the percentages, but ertainly it would be more profound perhaps even than New 'ork City.

DR. BROWN: What he said was that the bottom line ras that they would probably have to have a 50 percent donor ncrease of available donors.

DR. NELSON: Was that based on ten years? Was that based on a ten-year cut-off?

COL. FITZPATRICK: It was based on six months. Ten years wouldn't have any effect because most of the tours in Europe are 18 months to 3 years, although there are repeat tours. So, we would have to assess the impact but there would be less impact.

DR. BROWN: Yes?

DR. PRUSINER: I just wanted Jay Epstein to comment upon the authority of FDA because I was under a different impression.

DR. BROWN: With respect to?

DR. PRUSINER: When you said the FDA couldn't abolish the Euroblood program. I thought that they could do

that.

DR. EPSTEIN: Yes, let me state clearly that if the FDA recommends an exclusion based on residence or travel in Europe of whatever period, that ban would apply to any and all attempts to import blood that did not meet that criterion. In other words, we would take enforcement action; there would be no Euroblood, and it is within our authority.

DR. BROWN: But you would issue a guidance, a recommendation or a regulation?

DR. EPSTEIN: Well, we would issue a recommendation, which is the same thing as saying a guidance. However, in doing so, we would be taking the point of view that we felt that it was within the interpretation of the regulations, in other words, that we felt it was essential to assure safety, purity, potency of the products.

DR. BROWN: Right. So, basically it is a big stick but it hasn't been used. Eh? I understand what you are saying.

DR. EPSTEIN: Well, there is no current violation. In other words, the European imported red cells do meet all current U.S. standards. The facilities are licensed; they are licensed as facilities of the New York Blood Center. They are subject to all U.S. standards, including donor screening, use of U.S. approved tests, and we do inspect them to assure that they meet our standards. So, at the

present time, with the current standards, they are suitable products. If we change the standard and we argue that it is on the basis of the authority to assure safety, purity and potency of biologic products, including blood, then any such imports for human use for transfusion would become inviolate and we would take enforcement action. So, we can control our borders and we would regard as an enforceable policy.

DR. BROWN: So, if you issue a guidance on anything -- anything, then to not follow the guidance is illegal?

DR. EPSTEIN: No, that is not, in fact, true.

DR. BROWN: That was my point.

DR. EPSTEIN: Guidance, in and of itself, is not binding on the agency or on the industry. It is a statement of FDA's policy or interpretation of regulations. When an establishment seeks to deviate from guidance the presumption is that they will make a case before the agency and propose an alternative procedure. So, from a purely legal standpoint that is true. It is hard to understand what alternative might be proposed given the current scientific limitations but, yes, if there were proposals for alternatives from guidance they would be considered and they wouldn't be presumptively in violation.

DR. BROWN: Are you clear on that, Stan? It is sometimes amusing, and other countries sometimes find it

amusing that FDA typically issues guidances whereas other countries issue mandates. You know, I don't want to get into a long discussion about why we do that, but the fact is a guidance can be flaunted at least once, and not go to jail, and that "ain't" true in other countries.

DR. EPSTEIN: Again, this probably isn't the time and place to discuss the legal structure of what we do, but if we believe that the deviation from the guidance itself would constitute a violation of existing regulations, then it is, indeed, directly enforceable. That doesn't mean that it couldn't be challenged in court. And there are sort of, two levels. If it is a violation of the letter of the law in statute or regulation, then the issue in court is only whether it happened or didn't happen. If it is a matter of interpretation, then the issue in court is what we call a battle of the experts. So, there is a larger legal framework. I am only trying to explain that the issuance of a guidance does not automatically create the equivalent of an enforceable regulation. The guidance per se is not enforceable. However, if the guidance is a statement that we believe is violative of regulations or statutes, then it is.

DR. BROWN: It is a kinder, gentler way, Stan, and it is also democratic and it usually works because the blood industry pays attention to guidances. Yes?

DR. DAVEY: Yes, I think that is certainly true if

guidance is issued, for all intents and purposes the blood establishments follow it.

Just a couple of broader comments, if I could, Paul. The committee is being asked really again to make major and far-reaching decisions on really inadequate data, grossly inadequate data. It is a situation that the committee has faced in the past and done very well. Certainly, if we are going to make a decision to extend the ban to all countries with BSE it has to be all or none. I don't think we can nit-pick between countries. I am a little concerned, actually, about the last vote on France.

So, that is what has to be done. But I think we have to look at the data we do have and the transfusion data are reassuring, and continue to be reassuring about transfusion-transmitted BSE or vCJD. That is in Europe and certainly here, in the United States. And, there is a great experiment going on in the United Kingdom right now which we can watch with care to see what happens over there. That certainly is a country where we are going to learn our lessons from.

But what should we do here? I think we do have to look at the impact on blood supply incredibly closely, and that impact is real and it is documented. People are not crying "wolf" about this. This is a real problem. Last summer there were shortages, many shortages across the

country and I think it is important for the committee to also note that these are not just broad shortages, they are especially acute in group 0. Group 0 blood is in incredibly short supply year round, and last summer was desperately short in many areas.

The industry will lose more repeat donors and more plasma apheresis donors, I believe, as has been mentioned by other speakers, and I certainly support the efforts that the blood industry has made to get new donors. We have to get new donors but that is hard. The industry has been working on this for thirty years with dedicated professionals. It is hard to get new donors, The industry can do better. But to make up the shortfalls that will occur, especially in New York City and elsewhere, are going'to be monumental and very difficult. We have to talk to the people on the front lines and in the hospitals who are not going to be getting enough blood. It is a problem that will impact patient care.

So at least in my view, we certainly have to be responsible for the safety of the American blood supply. These are critical issues. The caution flags are flying high. But, it is not safe to not have enough blood. It is not safe to have people going with cancelled surgeries or worse in this country, and we have to approach these bans with great caution. And, I certainly hope the committee will certainly do that on this question.

DR. CLIVER: That was something that bothered me in the presentations this morning. It looks as if you could conclude from the zero slope of the inventory that absolutely nothing we do here is going to make a difference in available blood in the United States, and I can't accept that. I really have to believe that, given our present method of motivating and collecting, we are going to be shorter and shorter and shorter even with the constant inventory.

A high profile case of this week was Ted Williams' open heart surgery. I don't know how many units of blood they expanded on an 82-year old there. He is not at risk of transmissible spongiform encephalopathies. If there were a second level of blood that we could administer to people in that situation maybe it would take a little of the pressure off, but if we are doing a one-size fits all, zero risk blood supply, why, then we have to start applying some criteria for deferring recipients and, given his notoriety, he probably would never have gotten left out but it does make me wonder how much of somebody else's life we are going to expand on people of that age.

DR. LURIE: I appreciate all the comments made about the blood banking, but it is true also that the organization that represents 50 percent of blood donated in this country has come to a different conclusion. Although I

understand that there might be political things operating as well, I notice that the representative of the Red Cross seems to want to make a comment and so I would like to add to her the question of how is it given the data available to this committee, or are you aware of some data of which we are not aware, that you came to the conclusion that you did? What was your thinking?

DR. BROWN: Yes, you have been waiting patiently.

DR. FREAS: Could you state your name and affiliation for the transcript?

MS. FREDERICK: Yes, I am Jackie Frederick, American Red Cross. Let me address the three questions and one statement made. No, the Red Cross does not import blood from Europe, and has not, as far as I am aware, for many, many years. I think there was an instance back in the '60's or '70's. So, no, we do not.

Two, yes, we absolutely would help out New York Blood Center, as I believe every blood center in this room would. We are humanitarian, not-for-profit organizations and if we decide for safety purposes to take a step that reduces availability, I am absolutely sure that we will all come to the aid of patients anywhere who need it and the New York Blood Center.

Three, I was unaware of Dr. McCurdy's offer to help us expand collections in the Washington, DC area but

would be very, very happy to do that.

How did the Red Cross come to the decision that we could implement these deferral criteria for safety purposes and maintain the blood supply? I believe this is our fifth year of continuing to grow blood collections in this country, and we have been successful in doing that. I believe this is a great country with all the expertise that knows how to reach the public and consumers. We have shown it over and over, and it is just a matter of devoting the right resources and the right time and the right effort, as someone here said, to getting it done. We have done it.

On August 14th of this year, we instituted a change in procedures to go from an ear sampling to finger sampling to protect donor health. We immediately lost 6 percent of our donors, and we immediately made it up because we planned for it and took quick action. But we have serious shortages that have to be addressed.

MS. FISHER: I know I sound like a broken record but it is of paramount importance that we ensure the safety of the blood supply, that we ensure public confidence in the safety of the blood supply, and that we ensure that the confidence of the people in FDA's ability to ensure the safety of the blood supply, and the donor base problem is a separate issue. I agree with the American Red Cross, that can be addressed with making donating blood a priority, more

of a priority than it has been in society; making sure that those who donate are healthy and that we eliminate even a theoretical risk of contamination of the blood supply, especially with contaminants that we don't even thoroughly understand yet.

DR. BROWN: I think we will have just one more question, or two, or comment and then we will put this to a vote.

DR. BURKE: I would like to address the question as directly as possible. I see that the other countries in Europe that are BSE countries are a separate problem and different from France. France has the problem that it was a major importer of British beef and, as Bruce pointed out, there are two issues to decide upon. One, what was the risk of importation, and over the last 10 or 20 years did people eat potentially contaminated beef? And, two, is there currently an epidemic in which they are having exposure to contaminated beef?

For the rest of the countries, from the data that I have seen so far, over the last 20 years or so the other countries have had essentially zero or very low risk of ingestion of beef from Britain and the issue is in the last few years whether or not they have had exposure to their own endogenous BSE.

So, the phrasing here for a ban going back 20

years would be essentially irrelevant for most of these other countries because during that time, from all the data we have seen, they have had very little exposure to potentially contaminated material. So, my own feeling on this one is it wouldn't make a lot of sense to go back 20 years and, therefore, I couldn't endorse it.

DR. BROWN: It probably would make sense if you were moving along this direction and go back 15 years, however. It is not so much the imported beef, Don; it is the imported material that was fed to cattle. So, that is what caused the endogenous --

DR. BURKE: If that were the case, then we would apply the Lurie formula, that the risk is directly proportional to the number of infected animals in the country at that time.

DR. BROWN: Not at that time. Now. 1

DR. BURKE: Well, now, and there was no perceptible risk as measured by infected animals in these other countries at a time when the U.K. had a huge epidemic.

DR. BROWN: That is exactly right.

DR. BURKE: And, France had a spill-over from that, and there is no evidence that these other countries had a spill-over by importation of beef or beef products that were intended for human ingestion when we looked at the data on import-export.

DR. BROWN: Well, if you look at the data on import-export, for example -- 1 am not really disagreeing -- France is in a category by itself in terms of import-export. What I am saying is that beef is not the crucial matter; it is flours, MDM, stuff that went into cattle and that went into cattle in a big-time way starting about 1985.

DR. BURKE: Well, what matters is what goes into people.

DR. BROWN: Ultimately.

DR. BURKE: I think we are in agreement, but I think there is a delay so that in one case -- and this is going to come up when we talk about the armed services -- in one case you basically have what we are now calling a spill-over from the U.K. epidemic, and that has its own time period and the risk that we are trying to assign is based on some proportion of the U.K. risk which we are now trying to define.

Now, for these other countries what we are looking at are the effects or potential effects of a second wave and, there, there is a delay because the material had to get into the animals and then into the people potentially. And, so far we haven't even seen it in people yet in these other countries. So, it doesn't make any sense from that point of view to use the same cut-offs because just scientifically I think we are all accepting the same fact, that is, we are

ooking at two different phenomena. There is the U.K. henomenon and its spill-over, and then there is a second ave that may be visible now, or about to be visible, in the est of Europe.

DR. BROWN: Well, I see three categories. The U.K. bviously is one, and I really do see France as an ntermediate category. I mean, there are two very listinctive things about France that are not true at this ime for any other European country. One is that they have vCJD. They imported a huge amount of material that could ave been contaminated that went into their cattle and umans, much more than any other country in Europe.

DR. BURKE: But I think those two are related, and I think the direct human contact --

DR. BROWN: I do too.

DR. BURKE: But I think the direct human contact is what is unique, and I am just trying to separate that from the indirect contact, if you will, where it had to go through a second wave of infection.

DR. BROW-N: Last question. Ray?

DR. ROOS: We are zeroing in on specific countries, U.K. and France, and in this question there is a big lump and I am not even sure how many countries are on the USDA list --

DR. BROWN: Essentially all of Europe. Is that

right? I mean, it is alls of Europe.

DR. ROOS: Or what the specific numbers are with respect to BSE in those. Maybe Linda wants to comment about risk of other countries vis-a-vis France just to put things in perspective. But it is difficult for me to vote without the detail that we have and review with respect to France.

DR. DETWILER: Right now in the USDA list it is countries that are known to have BSE cases but, in addition, those that are high risk factors and that does include the entire Continental Europe.

To answer Dr. Roos' other question, it is difficult right now to make an assessment because of what Dr. Lurie has pointed out, which is that you really need to have this data over a denominator, and right now, because of the surveillance starting, you know, on January 1, you would still have a reported occurrence but that would give you some proportion because if you look at Portugal, it does stand out as far as cattle cases.

But you are still talking about a human factor here and what got into humans, and I still think exposure and/or SMBs are another thing to take into consideration.

DR. PICCARDO: I agree with Linda. The issue of Portugal is an issue that we should consider separate from the rest, I think. The fact that vCJD has not been diagnosed in Portugal doesn't mean -- I mean, maybe it is just a

failure in the diagnosis. I mean, we don't know. Portugal is a country that has a lot of cattle that is infected.

DR. BROWN: Allan, what would be the impact again on loss of donors if we just wiped out the whole of Europe for ten years?

DR. WILLIAMS: I don't have a ten-year value. At the five-year value, which we have, it would be approximately 0.7 percent.

DR. BURKE: That is donors traveling. That doesn't include Euroblood and I think that is important.

DR.. WILLIAMS: Correct.

DR. BELAY: The New York Blood Center -- I believe they told us that 25 percent of their blood supply would be cut off by using ten years because this essentially would be people who have resided in Germany, Switzerland and Holland, if I understand it correctly, that contribute to Euroblood. So, getting rid of 25 percent of the blood supply in New York, they told us, would be devastating for the New York area. I suggest that we give the New York Blood Center a chance to phase out their source of blood products from Euroblood and consider for the time being -- and this is a proposal for me -- consider for the time being the other high risk countries in Europe such as, for example, Portugal.

In Portugal, I agree with Linda and also Pedro,

has probably the highest risk of BSE in Europe, second only the United Kingdom. In addition, as far as know, Portugal had not implemented, for example, the over 30 months scheme probably until recently. So, the risk to humans in Portugal will probably be higher than many other European countries. So, I would propose potentially adding Portugal and possibly also Ireland because Ireland has a new vCJD case and probably frequent travel to the U.K., as evidence by that vCJD patient possibly contracting the disease in the United Kingdom. So, I would propose adding those two countries and leaving out the rest of Europe for a period of ten years.

DR. BROWN: Comments? Ray?

DR. ROOS: I wonder whether Dr. McCurdy wanted to comment on the situation in New York and what the impact would be, for example, if there was a ten-year ban with respect to all of Europe. What is your perspective on the impact on the New York area?

DR. MCCURDY: Well, I think that I am very concerned about supply in the U.S. as a result of a ten-year ban on all of Europe, and it is primarily making up the deficit in the New York BloodCenter. One question I was going to ask of Dr. Freas is it is my understanding that this committee, like BPAC, is supposed to deal with science and not supply, but it looks to me as though, in the absence of reasonably hard data, better data than we have or perhaps

movementtoward making up that deficit and reducing the dependence on Euroblood, I would be inclined to talk about the risk-benefit here being riskier to get rid of that blood than it would be to continue to use it, at least for a period of time.

DR. FREAS: I am sorry, I am going to pass it on to our policy experts to make a comment on that, not take it myself.

DR. NELSON: It is a separate question, but I can't see how we can separate this question from the impact on the military blood supply. It is inconceivable to me that we would have one set of criteria for the civilian population and another set of criteria for the U.S. military. To me, I think the adverse impact on the U.S. military blood supply which, you know, could face substantial needs, would probably be even greater than in New York City.

DR. BROWN: Yes, I think the military was separated because so much of its product comes directly from the U.K., you know, wherever they were.

DR. NELSON: Well, they are already following the U.K. ban, isn't that right, Jay?

DR. BROWN: In the U.K. they are.

DR. EPSTEIN: The point of clarification is this, that for the active duty military and dependents stationed

outside the U.K. in Europe the meat products were heavily sourced from the U.K. during the U.K. risk period.

DR. BROWN: Yes.

DR. EPSTEIN: So, they are already adopting the policy of deferral for residents or travel in the U.K. but the issue is exposures that occurred outside the U.K. attributable to U.K. beef.

Let me also clarify that the policy would not be different for the military and the civilian blood donor. The policy would be the same. It is whether an exposure due to being active duty military or dependent in Europe in the risk period should be a base of deferral. That would then be applied equally whether it was a civilian donation or a military donation.

DR. NELSON: Well, it could have a differential impact.

DR. EPSTEIN: Yes, that is true but it is not because the standard for donation is different. The impact would be different.

DR. BROWN: We have answered three questions. It is 1:30. We have.questions to answer before lunch. Either the FDA is going to have to punt on some of these questions and issues or we are just going to have to run through roll call votes. There is no way that this meeting will be over at this rate until midnight. So, I guess I should ask the

representatives of the FDA if they find it more valuable for us to continue discussing these things, you know, at some length and in detail and simply not address some of these questions because we will never get to them.

DR. EPSTEIN: I think we are happy to just call the vote.

DR. BROWN: Okay. The vote is on the question you see before you.

DR. LURIE: I want to ask a question about that, which is, my understanding of the question then since I may have blown it before, is does this mean that it would be all other countries identified by USDA? Are we talking about for all other countries? As soon as USDA identifies one of them as a BSE country, then you are out -- no distinction among them? That is what the vote seems to be on.

DR. BROWN: That is what the vote is on.

DR. LURIE: Which prevents those of us who might vote for some but not the others from offering a coherent vote.

DR. BROWN: Yes, but your comment is now on the record, being paid attention to by all of the FDA people in the room.

DR. LURIE: The FDA has a habit of doing that with my comments.

[Laughter]

DR. BROWN: So, as I understand the FDA's final decisions on these things, it is really not just a question of the vote; they really do look at the transcript and decide on balance what they ought to do. Yes?

DR. EWENSTEIN: Can I propose, because I think there is a consensus growing here, that if the vote comes out on this one no that there be a second vote on perhaps, as was suggested, on Ireland and Portugal as part (a) to this? I have a feeling that that will produce a different result.

DR. BROWN: Okay, let's do it. Let's vote on (a) as written. I have no problem with adding a second question phrased in that way. So, everyone who is voting will now understand that a no vote will not close the issue but that we will rephrase it with respect to (a) country or (b) country or (a), (b), (c). Ray?

DR. ROOS: No.

DR. DETWILER: No.

DR. EWENSTEIN: No.

DR. BURKE: No.

MS. FISHER: Yes.

DR. MCCURDY: No.

DR. FREAS: Dr. Burke said no, and Barbara Loe Fisher?

MS. FISHER: Yes.

DR. MCCURDY: No.

DR. PICCARDO: No.

DR. GAYLOR: No.

DR. NELSON: No.

DR. BOLTON: No.

DR. BROWN: No.

DR. BELAY: No.

DR. CLIVER: No.

DR. LURIE: No.

DR. WILLIAMS: No.

DR. PRUSINER: No.

DR. FREAS: I have one yes vote.

DR. BROWN: Okay. We are now voting on question 3(a) subset (1) which is exactly the same question, except now we say Portugal and Ireland. I want to be sure that the committee agrees that is a decent question to vote on, particularly those two countries. Everything else is the same. If you want to discuss it, it is okay with me. I mean, it is a brand-new question and it may not be one that the FDA loves. I don't know, but it has been a proposal. It seems reasonable and the restaurant closes at 2:00 p.m.

[Laughter]

I can say in view of that, for sure, we will not consider the military before lunch. For sure. This is going to be the last vote because I think (b) will be mooted. Is

the committee happy about those two countries as being identified as a group at the moment? We are talking about the Republic of Ireland and Portugal.

DR. BURKE: I am not entirely comfortable with this process right now. I am sorry. I don't see a sharp distinction between those two countries and it would be helpful if we could review the BSE prevalence per country before we made the decision that these were the two countries that we felt were so different.

DR. DETWILER: Paul, if I may, maybe I can help a little bit with Portugal. The European Union had a geographical risk assessment conducted and Portugal and the United Kingdom both were in category four, which is the highest risk. So that would give you some basis for that. The Republic of Ireland actually, in discussions, kind of was borderline. The remainder came in category three.

DR. BURKE: Okay. Again, it would be helpful to see the statistics, and I like looking both at the absolute numbers as well as the prevalence per unit population. I think both of those numbers would be useful to inform this decision. I am sorry if it takes longer but I think this is an important decision.

DR. ASHER: We have discussed briefly both countries in previous meetings. From the agency's point of view, I would say the only issue might be that we have not

reviewed either of those countries and their situation in any depth at this meeting.

DR. BROWN: Another problem is stipulating USDA category risk four --

DR. DETWILER: It is not a USDA categorization; it is the European Union's categorization. Actually, Ireland was classified in three. It ended up being in three but it was one that moved up and down a little bit.

DR. BURKE: I would also like to point out that these curves are about 0.001 or 0.01 of what the curves were in the United Kingdom at the height of the epidemic in terms of the total burden of infected animals. So, depending on how you want to express the risk to humans, as the prevalence per unit population or the absolute number of animals in a given area, I keep struggling for some measure of relative risk to human populations in the different countries and my own assessment, correctly or incorrectly, is that it is on this order of 0.01 of what it was for the United Kingdom, for which we have already established policies.

DR. BROWN: Linda, is the identification and separating out of these two countries a reasonable -- is it reasonable to pick these two countries? If we are going to pick on a country at all, what countries would you think present the greatest risk of having, you know, increasing

BSE numbers?.

DR. DETWILER: I think that is hard to predict, but I think the two countries for control measures for human health were very different and that might be a good point that David made and we would really have to go back and really look at those. I don't have that right off the top of my head. That is the bottom line, you are still talking about what the human population was exposed to.

DR. BROWN: Right.

DR. DETWILER: And when they put control measures in and how successful they are. I think that is really the bottom line. Peter said about looking at just cattle disease reported and then you can have countries that stick out, at least right now.

DR. BROWN: Right.

DR. DETWILER: However, the bottom line is they are different in that regard.

DR. BOLTON: I believe that those factors are included in the GVR assessment, and they came to the conclusion that those are really high risk countries.

DR. DETWILER: But the GVR did decreasing risk and static or increasing, and I think that is where you really have to look and, I apologize, I don't have this right at the top of my head with all these countries.

DR. BROWN: Well, we can vote on this question

because you can always vote no. I mean, these were two countries that several members of the committee thought might well be put in a different category and maybe most of us don't think that we have enough information to do that, but we can vote on it if the committee wishes to vote. I am not phrasing these questions. Does' the committee want to vote on the question separating out the Republic of Ireland and Portugal?

DR. ASHER: If the committee wants to rely on the scientific steering committee's geographic BSE risk, France is also a category three country and there are others. So, you have some justification for separating out those two category three countries from the others, if you wish to rely on the EC system.

DR. BROWN: That is why I asked Linda, do you think there is any basis for doing that? Is that a sensitive question?

DR. DETWILER: Again, I think the bottom line for this committee though is, you know, just using reported disease wouldn't tell you the whole story for this committee. The other thing with the Europe evaluated countries, they submitted data to them. So you would still have other countries that did not submit data.

DR. BROWN: On the other hand, I boxed myself in because I told the committee that we were going to have an

opportunity to vote on that question. So, we are going to vote on that question. So, the question is the same as the question which was already voted, should the FDA recommend deferral of blood or plasma donations from persons with a history of travel or residence in Portugal and the Republic of Ireland for an aggregate of ten years or more after 1980? That is the question. I will defer.

DR. DETWILER: I am going to vote no because I think it needs to be evaluated more.

DR. EWENSTEIN: Yes.

DR. BURKE: No.

MS. FISHER: Yes.

DR. MCCURDY: No.

DR. PICCARDO: Yes.

DR. FREAS: Dr. Piccardo was a yes. Dr. Gaylor?

DR. GAYLOR: Yes.

DR. NELSON: No.

DR. BOLTON: Yes.

DR. BROWN: No.

DR. BELAY: Yes.

DR. CLIVER: No.

DR. LURIE: Yes.

DR. WILLIAMS: No.

DR. PRUSINER: Yes.

DR. FREAS: The no votes are Detwiler, Burke,

McCurdy, Nelson, Brown, Cliver, Williams. Seven no votes. Eight yes votes. My apologies, there was one abstained. It was seven-seven and one abstained.

DR. BROWN: That really does it because it means we don't have to vote on question (b) --

DR. PRUSINER: No, no, we need a recount.

DR. BROWN: We all have to take the train south.

DR. PRUSINER: We need a recount. There are 16 of.

DR. FREAS: For the no votes it was my math that was off. The yes votes are Dr. Ewenstein, Barbara Loe Fisher, Dr. Piccardo, Dr. Gaylor, Dr. Bolton, Dr. Belay, Dr. Lurie and Dr. Prusiner, and that should be eight yes votes; seven no votes and one abstained vote.

DR. BROWN: So, eight yes, seven no and one abstention. That still moots question (b) so we are going to go to lunch.

DR. FREAS: What time will we be back?

DR. BROWN: Well, the restaurant closes at 2:00 so I guess we can be back at 2:15.

[Whereupon, at 1:35 p.m., the proceedings were recessed, to resume at 2:25, this same day. 1

AFTERNOON SESSIONS

Committee Discussion (continued)

DR. BROWN: We actually did not address a finial question in advance of the military personnel question, and this was touched on earlier, about aggregates of residence in various countries. So, we are skating on even thinner ice here and the question is should deferral of blood or plasma donors be recommended based on some combined aggregate duration of travel or residence in more than one BSE country? If so, how should that be estimated appropriately? Well, that certainly silenced the committee.

[Laughter]

DR. LURIE: I will take it; I can comment. I am not necessarily putting this forth because I realize that it is a question of, in effect, how do you add apples and oranges. That, in effect, is what the question is.

If there is any rational basis, and I am not sure that this is it, to the extent that we implicitly echo the 1 in 20 relative risk estimate by going with six months and 10 years, I suppose one could put forth something that amounts to, you know, Britain plus 0.2 of other countries. So, that is the only rational thing I can come up with.

DR. BROWN: That is exactly right. There is only a single rational way to do that based on what the committee has already recommended. I guess the question is whether or

not that is in any way practical, because if it is not practical there is no point in doing it. We have Sue, who could probably tell us whether or not anything of this nature is even within the realm of possibility.

DR. LEITMAN: I think that the more complicated, complex questions the donors get -- remember that they are not always asked by skilled, experienced nurses. There are sometimes technical people whoa re not that experienced in asking these questions or not that skilled -- the more you ask questions of this nature, the less attention may be paid to more critical questions about donor safety because you only have a limited time in the donor screening booth. So that is a concern.

I can't imagine "X" months here plus "this" months here, plus so many months "there" in some algorithm would be practicable. Ten years in one country and the existing six-month deferral would be, but to add them together I think would not work.

DR. BROWN: Yes, I suppose the question could be phrased, have you ever visited Great Britain and, if so, for how long? It is already a complicated question. Cumulative time since 1980, and then have you ever visited other countries in Europe and cumulative time since 1980? Then, the questioner would have to do some arithmetic.

DR. LEITMAN: But different periods. One period is

1980-1996, and another one may start at 1985 and extend to present --

DR. BROW: Or '80 to the present. Yes, it is a little different. Anybody on the committee? Yes, Don?

DR. BURKE: Again, I can't see that there is any additional risk from having lived in, say, Portugal between 1980 and 1994. There is no data that says that Portugal had any substantial risk either through importation of beef from Britain or their own BSE herds. So, to have criteria that adds cumulative years where there is no apparent risk whatsoever would just seem illogical to me.

DR. LURIE: Don, it seems illogical but you voted against the extension of the ban. So, to me, we have to work now from the assumption that the previous decisions were rational.

DR. BROWN: Always a risk thing to do, yes.

DR. LURIE: Like I said, an assumption. I am not sure it is quite as complicated as you say. The way the questions would go is have you been in Britain for six months between such-and-such a period. If the answer is yes, then you skip any questions about the rest of Europe because it is irrelevant. Right? Then, the next question is have you been to these other European countries for such-and-such a period? Firstly, have you been at all, and if the answer is no, then that is the end of that. If the answer is yes, then

you get some number and then the questioner just has to divide that by 20, or whatever it is, and add the previous two numbers.

DR. BROWN: Yes, it is that third possibility --

DR. LURIE: Yes but, remember, it is the responsibility of the questioner not the questionee. Right?

DR. BROWN: Except to the extent that Sue implied that --

DR. LEITMAN: There is all sorts of confusion that comes up. We found a donor screener deferring everybody who lived in the Falklands because that is part of the U.K., or she thought it was. So, are the Azores Islands part of Portugal? I am just thinking of extensions of this. It can get very complicated.

DR. BROWN: Both are right on both counts. They both have BSE and you are right about their country of attachment. Good for you. I wouldn't have thought of that.

DR. BURKE: I would like somebody to explain to me why there is additional risk between 1980 and 1990 in any of these countries. Just tell me why we want to count that in any risk formula. What risk is there whatsoever from these countries?

DR. BROWN: From 1980 to 1990 --

DR. BURKE: Or even 1995, but just give me the first decade.

DR. BROWN: Let's say country "X" imported from Great Britain quite a lot of meat and bone meal that they then fed to their own cattle. Okay? They did this in, say, 1983.

DR. BURKE: Give me a specific instance of what information you have that will allow you to --

DR. BROWN: No, you are asking me under what circumstances "might" and I am telling you under what circumstances "might". Now they got a few cattle that have BSE. They are incubating BSE because they have been infected by the meat and bone meal imported from Great Britain. But they are slaughtered. They are not recognized as having BSE. Now they are slaughtered and they are recycled in the rendering plants, and this is the beginning of an outbreak of BSE. Not only are they slaughtered but their carcasses, their meat and everything else is going into the human food chain.

DR. BURKE: So, you are willing to make the backwards extrapolation that if they have BSE today, they had it sometime between 1980 and 1990.

DR. BROWN: As I said before, I think '80 is pushing it but I think it is entirely possible that any one of a number of countries in Europe had BSE unrecognized before 1990.

DR. BURKE: I can't refute that possibility.

DR. NELSON: Are we asking a blood bank or omebody to add up four months and 23 days in the U.K., a wo-week trip to the Falkland Islands and divide something y 20 -- I mean, we are going to have to have computer iterate --

DR. BROWN: No, you know what we should do? We hould do this as a pilot project and see what happens in ne or two centers.

DR. KATZ: As we speak, we are implementing a omputer interactive donor screening package in my blood enter, and as we have figured out what would work well, the ey thing that we realized immediately was that there had to e no keyboard available to the donor; that it had to be a ouch-screen yes/no only, and then we have trained personnel rho will review the answers off the computer. So, I mean even in that system, which I think is getting kind of close to the way we ought to be doing things generally, it adds an extra level of screening. Where we used to have no turnover in our donor room, with the tight labor market we now have enormous turnover. These are barely above minimum wage jobs and the error and accidents in this labor tight market, just with the yes/no questions we use now, have gone up four- or five-fold -- Clinton's revenge for a good economy, or something. I don't really understand it. But this is daunting. This concept is daunting.

DR. BROWN: Dr. Cliver?

DR. **CLIVER:** Further to confuse the issue, the atter of who was using meat and bone meal in the U.K. and ow much of it is not a continuous variable. Apparently round the time that they decided that those materials ouldn't be recycled to British cattle, some of the owners hereof in the U.K. did a marvelous job of selling those ame material to Continental Europe. So, we have some mportation figures in the reading I received before I came, ndicating that a few target northern European countries got ay more of that material from the U.K. right after the ban n Britain than they had ever had before. So, there was a udden perturbation in whatever had been the baseline.

DR. BROWN: Yes, that is absolutely right. The ther point that I suppose is amusing to make is that witzerland is one of the countries with the largest number f cases, and according to the import-export figures they ere a very trivial importer of all the things we have been alking about. So, there is no direct proportionality. Bruce?

DR. EWENSTEIN: I was going to say I think we shouldn't go back to the old debate. Obviously we were very divided on most of Europe and the FDA is just going to have to hear that divided opinion and come up with their own opinion. But if we just look at our vote on France, for

example, and just limit this discussion to if we are going to do algebra between exposure in the U.K. and exposure in France or not. We heard from the Canadians and, as I understand it, they decided not to. I think it is a matter of practicality rather than science. I mean, it would make sense, if we just agree on France as being an extension of the U.K. epidemic, to have some sort of algebra that would add the two.

I know you said it as a joke, but I think piloting this makes some sense rather than trying to institute it across the country in a way that just may not be practicable. It makes sense to see if we could recommend that something like this be tried and if it just can't be done, it can't be done.

DR. BROWN: No, I was serious. I smile sometimes when I am serious.

DR. ROOS: I think it is going to be difficult for the donors to figure out -- 1 think there is probably some difficulty to know whether it is before six months or after six months, but when you start saying before six months, how many months? I mean, just thinking about myself, you know, I know I have been in U.K. less than six months over the last twenty years but if you ask me how much time in order to get this algorithm together, then it is very difficult. So, I just don't think it is feasible because we need some

accurate numbers in order to add them together and we are starting with something relatively rough to begin with. So, it is fine to do a pilot, Paul, but I think it is going to be a problem.

DR. BROWN: The other thing that would be interesting to do, which won't ever be done, is to try and verify in a pilot study just exactly whether or not their estimates of the time accumulated in, say, the U.K. is accurate. My guess is there is a gray zone of several months where some might get excluded and some would be included, If you spent ten years or a year in the U.K. there is no problem.

Shall we vote on this question? Again, the question is should deferral of blood or plasma donors be recommended based on some combined aggregate duration of travel or residence in more than one BSE country? If so, how should that be estimated appropriately? Sue?

DR. LEITMAN: No.

DR. BROWN: Sue says no.

DR. WILLIAMS: No.

DR. FREAS: Dr. Williams was no.

DR. LURIE: Yes, I would like to see a pilot test.

DR. CLIVER: No.

DR. BELAY: No.

DR. BROWN: No.

DR. BOLTON: No.

DR. NELSON: No.

DR. GAYLOR: Yes.

DR. FREAS: That was a yes. Dr. Piccardo?

DR. PICCARDO: No.

DR. MCCURDY: No.

MS. FISHER: Yes.

DR. BURKE: No.

DR. EWENSTEIN: Yes, in a pilot program.

DR. DETWILER: No.

DR. ROOS: No.

DR. FREAS: The four yes votes I have are Dr. Ewenstein, Miss Fisher, Dr. Gaylor and Peter Lurie. All other votes were no votes, for a total of 12 no votes, four yes votes.

DR. BROWN: Well, in principle our votes on the military personnel should be a piece of cake because we cannot diverge from what we have already decided for Europe as a whole, but I may be wrong and we will see. Should the FDA recommend deferral of blood or plasma donations from persons with a history of six months aggregate potential exposure to U.K. beef and beef products during service or dependent status in the U.S. military in Europe from 1980 to 1996. Discussion? Bruce?

DR. EINSTEIN: Well, it seems to me that we all

ccept the fact that the human disease is based on some nvironmental factor that was existing in the U.K. I think ost of us accept the fact that it was probably ingested. If o, then the risk to the U.S. personnel in Europe would ollow in some proportion to their food exposure rather than o where they were actually stationed. But they weren't as ully exposed to the U.K. food environment as those living n the U.K. It was some proportion. I know we hate to have a ot of different rules but in this particular case it may be ery important to try to a little bit more accurately define hat that risk was. I would have to go back and look at the umbers that were presented to us, but if there was, for xample, a 10 or 20 percent exposure to that food nvironment, then I would think that the risk to those ersonnel would be proportionate to that risk and we could, hen thinking about blood donations, use that same roportionality, much the same way that we have tried to stimate the risk in France.

DR. BROWN: Yes, I think one of the problems is that what we saw presented was itself not uniform. That is, northern Europe -- it is like Hannibal, north of the Alps and south of the Alps, different intakes, different suppliers. I mean, in once case U.K. from '85 to '90 went to U.S. and in the north and didn't go in the south. The proportionality of beef coming from the U.K. differed in

different commissaries. If the military representatives would like to comment on the possibility of estimating any ind of rational proportionality of risk based on what they ave heard this morning, I would be happy to listen. I know hat is not a happy question and it is not meant to put you n the spot. In fact, you might perfectly well say bsolutely impossible; you are out of your mind.

COL. SEVERIN: To accurately come up with an stimate of risk would be almost impossible. The best that 've could find out for potential consumption for the commissary sales, which would be all your family members and their spouses, 35 percent of the beef they would have consumed could have come from the U.K. Soldiers living in the barracks -- there is no way to know how much of the time they ate in the mess hall, which would have been U.S. meat, how much of the time they went down the snack bar or went off the installation to eat locally. There is no way to come up with that type of estimate.

When you look at the numbers that were in the cafeteria or the other short, quick 7-Eleven type outlets, 20 percent of that beef came from the U.K. over that entire 16-year span.

So, like you say, it varies because of the way the products were procured. So, there would be no way to put an accurate risk number on it.

DR. BROWN: If one were to, nevertheless, try you could probably say something in the range of 20-35 percent, in this range, might have come from the U.K.

COL. SEVERIN: Yes.

DR. BROWN: Over the time period that we are talking about, no matter where the base was in Europe, that is south or north of the Alps.

COL. SEVERIN: Looking at it as a potential worst case, yes, I would go along with that.

DR. NELSON: But given the population size of the military and the population size, say, of France and the importation, is there any evidence that more people would be exposed in the military than would be exposed from British beef that went to France or Germany? I mean, I am not sure that we can really define that this risk is greater.

DR. BROWN: What was your total? It was about 4.5-5 million people over the entire span of 15 years?

COL. SEVERIN: Right, 4 million, 4.4 million over a 16-year span.

DR. BROWN: Right. So, that is about a fifteenth of the population of France, for what that is worth but I don't think it is worth anything.

DR. NELSON: If France imported 10 or 20 percent of the among that the U.S. military imported and consumed then the exposures would be equal.

DR. BROWN: Yes?

MS. FISHER: As a former military dependent who spent four years in Europe as a teenager in the 1960's, obviously not during this time period, I remember well that we were sort of totally dependent upon the commissary food but at every opportunity we went out to the local economy and consumed the restaurant food.

But, please correct me if I am wrong, the only identifiable U.S. population and traceable U.S. population that has been exposed to **beef** or beef products from the U.K. is the troops and the military dependents who lived in Europe between 1980 and 1996. And, I we like to know how aggressive and comprehensive the surveillance has been to look for symptoms of vCJD in this U.S. population because I think that might change things, although I do think it is clear that this population had a much greater exposure than the general U.S. population.

DR. BROWN: Well, that is certainly true and my guess is there has been a good deal of diagnostic acuity spent on this issue. Am I right, Colonel?

COL. FITZPATRICK: The Department of Defense has a reportable disease database, of which new vCJD is not a part. However, all of our bases and installations conform with local policies on reportable diseases. So, while there isn't a program of active surveillance monitored by the

Department of Defense for vCJD, our facilities participate in the local requirements of CDC and the local county laws and state laws on reportable and surveillable diseases. So, we should be about equal to the rest of the United States in monitoring for that.

MS. FISHER: The reason.1 asked the question is because there has been some discussion here today about the countries which were not doing active surveillance, and when they found far more cases.

DR. BROWN: This is with respect to cows. Active surveillance of CJD has been going on in Europe, big time, for six years.

MS. FISHER: I am sorry, I thought it was for both animals and humans.

DR. BROWN: No. Just as a thought, I think it would be a good idea if the military really paid attention to the possibility of vCJD occurring in their population that has spent time in Europe, especially the population that is no longer on active duty.

COL. FITZPATRICK: They are being seen --

DR. BROWN: Well, they are probably being seen by VA hospitals too.

COL. FITZPATRICK: Well, they are not necessarily all retirees.

DR. BROWN: No. The point is that I think we are

all worried that if we have a case of vCJD in an American that a military person is a prime candidate.

COL. FITZPATRICK: We can take that back with your concerns and I think that we will be interested in that and, obviously, we answered a lot of questions yesterday concerning that.

DR. BURKE: As a point of information, the Institute of Medicine does have a panel now on disease surveillance in the military as being at a high risk for a number of emerging infectious diseases that may be found in higher incidences in other parts of the world, and I will make a point that this is included in that report.

DR. LURIE: I tend to think that it is going to be very difficult to quantify that six months may simplify things but it is probably okay. What we haven't really talked so much about is the flip side of this, which is the impact upon the blood supply for the military. As I understood the presentations from the military, the rate of blood donation was higher among military personnel, and I also thought one of the gentlemen who presented implied that it would, if anything; be easier to supplement that than is generally true in the civilian population. So, that part of it gives me some reassurance as well.

COL FITZPATRICK: If I implied it was easier, I am not sure I was correct in doing that. The rate of donation

is higher in our population. Our recruitment may be more aggressive. Our recruitment may be more successful. If this is a six-month deferral we have to replace 19,500 donors annually in order to maintain our current collection rate. As had of the blood program, I consider that doable, certainly not easily but I consider that doable.

DR. BROWN: As Dr. Nelson said, however, 'if we are going to follow strict proportionalities we are certainly not talking about six months. The maximum we would be talking about would be a third of the possible exposure, which would be 18 months or 24, you know, like two years, which might make it much easier for you if the committee goes that route.

COL. FITZPATRICK: Given the tour lengths in Europe, a single, unaccompanied tour ranges from 18-24 months. An accompanied tour is usually three years and can extent out to five or seven years depending on if the person comes back.

DR. BROWN: So, it wouldn't make much difference. Six months and 18 is essentially the same for you.

COL. FITZPATRICK: Twenty-four can make a difference; 18 and six are probably about the same.

DR. BROWN: Right.

DR. BELAY: I was going to comment on the possible occurrence of new vCJD in the United States. I think there

is plenty evidence that new vCJD has not been detected in the United States. As you know, CDC had instituted several surveillance mechanisms to specifically look for the occurrence of new vCJD in this country. These mechanisms include the establishment of a national center, which we call the National Prion Disease Pathology Surveillance Center. Dr. Gambetti is in the audience and he is the director of it. They have systematically been testing brain tissues from patients diagnosed with CJD or suspected with CJD and they have not been able to detect the occurrence of new vCJD in this country.

But this does not necessarily apply, for example, for military personnel that may have been stationed outside the United States in different parts of the world. We would be willing to work with the military to set up a system of potentially, you know, searching for those cases among the military.

DR. EWENSTEIN: I was going to say the same sort of principle that we used for the general population of trying to find a break-point at which you could eliminate a substantial amount of risk and have an acceptable amount of impact on supply would make sense. I think it would be reasonable to have the military do their own analysis on that, but it does sound like you could justify, based on this proportionality concept, two-or three-year type of

deferral lengths of time which would happily seem to eliminate a lot of folks who were doing single tours. Again, you would actually have to look at the numbers to come up with something that was truly optimized, but I think that would be my advice, to try to find a point around that two- or three-year time frame.

DR. BROWN: I think we can probably vote on question (a) because I don't think anybody thinks six months is worth anything,

DR. BURKE: A good number of these people in the military will leave the military and then be civilians, and they will donate there as well. So, the same question will come up, will that be a question for civilian blood banks. I think we can't divorce the military blood bank question from the civilian blood bank question.

DR. LEITMAN: I was just going to comment on that. I thought we heard data this morning that if you take these 4.4 million young adults, patriotic young adults who donate at a higher frequency than other persons of that age in America that the loss to the civilian donor supply was going to be on the order of 3 percent. Was that Dr. Williams who gave us that? Because 3 percent is very sizeable.

COL. FITZPATRICK: That was Allan's estimate, and he adjusted for age of that population.

DR. LEITMAN: Three percent is sizeable.

DR. BELAY: As a reminder, what would the impact on the military blood supply be?

COL. FITZPATRICK: With the six-month deferral, 15 percent of our population becomes ineligible to donate. Again, to maintain our current collections, that means i have to replace about 19,500 donors a year out of our active duty population of **1.4** million.

DR. BROWN: Let's vote on part (a) and then we can get to part (b). So, should the FDA recommend deferral of blood or plasma donations from persons with a history of six months aggregate potential exposure to U.K. beef and beef products during service or dependent status in the **U.S.** military in Europe, from 1980 to 1996? Ray?

DR. ROOS: No.

DR. DETWILER: No.

DR. EWENSTEIN: No.

DR. BURKE: No.

MS. FISHER: I just want to clarify something, are we taking another vote on another time frame?

DR. BROWN: Part (b) of that, if not, do members of the committee suggest some other policy for deferral? So, we will be voting on that and that would obviously include the possibility of a time frame policy.

MS. FISHER: I am going to vote yes.

DR. MCCURDY: No.

DR. PICCARDO: Yes.

DR. GAYLOR: No.

DR. NELSON: No.

DR. BOLTON: No.

DR. BROWN: No.

DR. BELAY: No.

DR. CLIVER: No.

DR. LURIE: No.

DR. WILLIAMS: No.

DR. PRUSINER: Yes.

DR. FREAS: I have three yes votes, Miss Fisher, Dr. Piccardo and Dr. Prusiner, 13 no votes and zero abstained.

DR. BROWN: Part (b) of that question is if not, and we voted not, can the members of the committee suggest some other policy for deferral of U.S. military personnel or dependents due to exposure to U.K. beef products?

DR. PRUSINER: I voted yes because I think that trying to make this 18 months, 2 years, 12 months is splitting hairs about a subject that we really don't know a great deal about, and I just think that we are putting a level of precision into our thinking that doesn't belong there. So, if we have picked this number of six months, people don't want to change it; they have left it alone for the U.S. To turn around and now say that we have a better

ay of judging this by putting 12 months or 18 months to his just doesn't seem to me to be at all rational. I think hat we have absolutely no reason to do that. And, if we are orried about replacements, we have heard that 18 months and months are the same. Then to turn around and say, well, ou know, we are going to try to help the military a little it and we are going to make it 24 months so we can cut it own a little bit more -- this, to me, is just totally rrational. So, I think we ought to just leave it at six onths and that is why I voted yes.

DR. BROWN: Other discussion? Comments?

DR. GAYLOR: The rationale seems to be that about third of the beef came from the U.K. for service and that s where the factor of 3 comes from for going from 6 months o 18 months. But, of course, there is beef consumption ther than on base so it is a factor too. So, maybe you ould go to the 12 months. But there is some rationale and logic based on what we have done in the past. If we are still trying to be logical, there is some reason to extend it.

DR. PRUSINER: How did we get to six months? Let's don't for a minute believe that six months is based upon the amount of beef. Six months is based upon coming to a number that the blood supply can tolerate. So, let's not start with that assumption and then turn around and make assumptions